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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 08/03/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/986,234	LAZAR, MITCHELL A.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 February 2005 and 08 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-4,9-11,23,24,34,82 and 83* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-4,9-11,23,24,34,82 and 83* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group VIII, without traverse, in the paper filed 2/22/05, is acknowledged.

Claims 2-4, 9-11, 23, 24, 34, 82, and 83 are being acted upon.

2. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the consensus sequence of Figure 18 must be identified by SEQ ID NO:. Applicant is advised that the consensus sequence is neither SEQ ID NO:2 nor SEQ ID NO:4; it is a separate sequence. For example, the largest fragment of the second line of the sequence would be C(S/T)CGSACGSWD(I/V)R. This sequence in neither SEQ ID NO2 nor is it SEQ ID NO:4.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 2-4, 9-11, 23, 24, 34, 82, and 83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically:

A) It is unclear precisely what is encompassed by the term "synthetic" antibody in Claim 23. The term is undefined in the specification. What is known however, is that by placing the term in an alternative, Markush type, grouping with a polyclonal antibody and a monoclonal antibody, it is clear that a synthetic antibody is neither of those.

B) The "an" in line 2 renders Claim 34 ungrammatical. Additionally, it is unclear whether the "fragment thereof" of the claim refers to the antibody or the resistin polypeptide of the claim.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 2-4, 9-11, 23, 24, 34, 82, and 83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for,

a method of treating or alleviating type II diabetes comprising administering to a patient afflicted with type II diabetes a composition comprising an antibody that binds the resistin encoded by SEQ ID NO:2 or SEQ ID NO:4 in an amount sufficient to reduce serum glucose,

does not reasonably provide enablement for,

a method of treating or alleviating type II diabetes comprising administering to a patient afflicted with type II diabetes a composition comprising an antibody that:

A) binds to a fragment of resistin, or

B) binds to a resistin encoded by a nucleic acid that shares at least about 30% sequence identity with a nucleic acid encoding a resistin, or

C) binds to a resistin that shares at least about 30% sequence identity with the sequence of SEQ ID NO:2 or SEQ ID NO:4.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to

that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

It is well-established in the art that function cannot be predicted based solely on sequence similarity to a protein found in the sequence databases. It is also well-established that whether or not functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences cannot be predicted by sequence alone. Attwood, (2000) teaches that, "it is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences". Similarly, Skolnick et al. (2000) teaches that the skilled artisan is well aware that assigning functional activities for any particular protein, or protein family, based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins. Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the related proteins. Note that even single amino acid differences can result in drastically altered functions between two proteins. See, for example, Metzler et al. (1997) wherein the authors show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86.

Bork (2000) states that the error rate of functional annotations in the sequence database is considerable, making it even more difficult to infer correct function from a structural comparison of a new sequence with a sequence database. Such concerns are echoed by Doerks et al. (1998) who state that: 1) functional information is only partially annotated in the databases, ignoring multi functionality, resulting in underpredictions of functionality of a new protein, and 2)

overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997) remark that there are numerous cases in which proteins having very different functions shared structural similarity due to evolution from a common ancestral gene. Brenner (1999) teaches that accurate inference of function from homology must be a difficult problem since, assuming there are only about 100 major gene superfamilies in nature, then most homologs must have different molecular and cellular functions. Bork et al. (1996) teaches that the software that assigns functions to new proteins often assigns a function to a whole new protein based on structural similarity of just a small domain of the new protein to a small domain of a known protein. Such questionable interpretations are written into the sequence database and are then considered facts.

For these reasons, the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity over the full length of SEQ ID NOS:2 or 4 to share the same function as the polypeptides of SEQ ID NO:2 or 4. Accordingly, the skilled artisan would not reasonably expect treatment with an antibody that binds polypeptides that are essentially unrelated to the resistin of SEQ ID NO:2 or 4 to provide an effective treatment for type II diabetes.

Regarding the polypeptide fragments of the claims, it is noted that the claims recite no size nor functional limitations on said fragments. Accordingly, the claims encompass fragments as small as 6 or 8 amino acids (the minimum epitope to which an antibody can bind). Again, the skilled artisan would not reasonably expect treatment with an antibody that binds peptide fragments that are essentially unrelated to the resistin of SEQ ID NO:2 or 4, e.g., a 10 amino acid peptide sharing just 3 amino acids with the resistin of SEQ ID NO:2 or 4, to provide an effective treatment for type II diabetes.

In total then, it is the Examiner's position that the specification fails to enable one of skill in the art to use the method of the instant claims, as broadly claimed, to provide an effective treatment for type II diabetes, without undue experimentation.

7. Claims 2-4, 9-11, 23, 24, 34, 82, and 83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Under *Vas-Cath, Inc. v. Mahurkar* , 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in *possession* of the invention, and that the invention, in that context, is whatever is now claimed.

There is insufficient written description to show that Applicant was in possession of an antibody that:

A) binds to a fragment of resistin, or

B) binds to a resistin encoded by a nucleic acid that shares at least about 30% sequence identity with a nucleic acid encoding a resistin, or

C) binds to a resistin that shares at least about 30% sequence identity with the sequence of SEQ ID NO:2 or SEQ ID NO:4.

Regarding the fragments of the claims, it is noted that none of the fragments are disclosed. Neither are any of the resistins sharing a percent sequence identity with the resistins of SEQ ID NO:2 or SEQ ID NO:4 disclosed. Again note that the only limitation set forth in the claims is that the proteins and fragments share about 30% homology with the resistins of SEQ ID NO:2 or SEQ ID NO:4. Clearly these proteins and fragments would comprise a genus of essentially unlimited size and unrelated function. And again note that as regards the resistins of part C), said resistins could be 100% non-identical with the resistins of SEQ ID NO:2 or SEQ ID NO:4 and still meet the limitations of the claims. Accordingly, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the genus of resistins to be bound by the antibodies employed in the method of the instant claims. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

8. Claim 83 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter

rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, a method wherein the amount [of antibody] inhibits production/expression of resistins.

Applicant fails to indicate where in the specification support for the limitation of the claim can be found. A review of the specification discloses only the use of a resistin-inhibiting amount of antibody.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 2-4 and 9-11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Ofei (1996).

Ofei et al. teaches a method for treating type II diabetes (NIDDM) comprising administering to a patient an antibody that binds to a resistin encoded by a nucleic acid that shares at least about 30% sequence identity with a nucleic acid encoding a resistin, or binds to a resistin that shares at least about 30% sequence identity with the sequence of SEQ ID NO:2 or SEQ ID NO:4 (see particularly page 882, column 2, first full paragraph). Note that given the breadth of the claims an anti-TNFα antibody employed in the reference can be considered to bind a resistin encoded by a nucleic acid that shares at least about 30% sequence identity with a nucleic acid encoding a resistin, or binds to a resistin that shares at least about 30% sequence identity with the sequence of SEQ ID NO:2 or SEQ ID NO:4.

The reference clearly anticipates the claimed invention.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The

examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Additionally, the Technology Center receptionist can be reached at (571) 272-1600.

1/31/05

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